## REMARKS

Favorable reconsideration, reexamination, and allowance of the present patent application are respectfully requested in view of the foregoing amendments and the following remarks.

### I. CLAIM STATUS & AMENDMENTS

As correctly stated in the Office Action Summary, claims 1-9 were pending in this application when last examined. Claims 1-9 have been examined on the merits, and stand rejected. The present amendment amends claims 1, 3, and 5-9 and adds new claims 10-16. The present amendment also cancels claims 2 and 4 without prejudice or disclaimer thereto. Claims 1, 3, and 5-16 are pending in this application. Applicants reserve the right to file a continuation or division application on any canceled subject matter.

Support for the amendments to claim 1 can be found in the Specification, for example, at page 5, lines 16-23, page 6, lines 2-6, page 11, lines 21-25, page 13, lines 28-29, page 35, lines 11-19, Tables 1-2 at pages 47 and 48, Example 5, page 57, Example 7 (Tables 7-9), pages 64-66, and in original claim 4. Support for the amendment to claim 3 can be found, for example, in original claim 3. Support for the amendment to claim 5 can be found in the Specification, for example, at page 6, lines 15-18 and in original claim 5. Support for the amendments to claims 6, 7, and for new claims 10-12 can be found in the Specification, for example, at page 5, lines 16-23, page 6, lines 2-6, page 8, line 22 to page 9, bottom line, page 11, lines 21-25, page 13, lines 28-29, page 35, lines 11-19, Example 5 at page 57, and in original claims 6 and 7. Support for the amendments to claims 8, 9, and for new claims 13-16 can be found in the Specification, for example, at page 7, lines 10-30, page 8, line 25 to page 9, line 31 and in original claims 8 and 9. Therefore, no new matter has been added by this amendment.

## II. FORMAL MATTERS

### A. Applicants' Priority Date

Acknowledgment has been made for the claim of foreign priority under 35 U.S.C. § 119(a)-(d) or (f), as well as the receipt of all certified copies of the foreign priority documents. See June 25, 2003 Office Action page 1, Item 13.

### B. Objection to the Specification

The Specification has been objected to for allegedly containing grammatical, idiomatic, and spelling errors. See June 25, 2003 Office Action, page 2. Applicants respectfully request that this objection be held in abeyance until there is an indication of allowable subject matter.

## III. REJECTION UNDER 35 U.S.C. § 112, SECOND PARAGRAPH

Claims 1-9 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. See June 25, 2003 Office Action, pages 2-3.

Claims 1, 2, 4, 6, 8, and 9 have been amended to remove the terms "trypsin-related" and "trypsin-like."

The phrase "the Sequence Listing" has been removed from claims 3 and 5, thereby obviating the Examiner's concern that the phrase lacks antecedent basis and is superfluous.

Claims 6 and 7 have been amended to include a positive recitation of method steps as suggested by the Examiner.

Claim 8 has been amended to recite "the" monoclonal antibody instead of "a" monoclonal antibody as suggested by the Examiner. Claim 8 has also been amended to remove the phrase "effective amount."

The Examiner contends that it is allegedly unclear whether claim 9 further limits claim 8. Applicants respectfully traverse this rejection. As discussed in the Specification at page 12, lines 4-10, active canine trypsin may exist in vivo in complex forms wherein trypsin is coupled with inhibitors such as α1-anti-trypsin and α2-macroglobulin. Thus, claim 9 further limits claim 8 by delineating the different forms of trypsin, such as trypsin coupled with inhibitors.

Therefore, in view of the foregoing amendments and/or remarks, Applicants respectfully request the withdrawal of these rejections.

## IV. REJECTION UNDER 35 U.S.C. § 101

Claims 6 and 7 stand rejected under 35 U.S.C. § 101, because the recitation of a use without allegedly setting forth any process and/or method steps results in an improper process claim. See June 25, 2003 Office Action, page 2. Applicants have amended the claims to recite positive method steps. Since the present amendment obviates this rejection, Applicants respectfully request the withdrawal of this rejection.

## V. REJECTIONS UNDER 35 U.S.C. § 102

### A. Hermon-Taylor

Claims 1-9 stand rejected under 35 U.S.C. § 102 (b), as allegedly anticipated by Hermon-Taylor et al., U.S. Patent No. 5,356,781 ("Hermon-Taylor"). See June 25, 2003 Office Action, page 4. For the following reasons, Applicants respectfully traverse this rejection as applied to the amended claims.

Hermon-Taylor fails to anticipate the claimed invention because the cited prior art reference fails to teach each and every element of the claimed invention.

To anticipate a claim, a cited prior art reference must either expressly or inherently teach each and every element of the claimed invention. Verdegaal Bros. v. Union Oil. Co. of California, 814 F.2d 628, 631, 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987); See also, M.P.E.P. § 2131.01.

In the instant case, Hermon-Taylor does not disclose nor suggest a monoclonal antibody ("mAb") specifically reactive to canine cationic trypsin or canine cationic trypsinogen, but non-reactive to canine anionic trypsin or canine anionic trypsinogen. Instead, Hermon-Taylor teaches methods for "measuring levels of released activation peptides using specific C-terminally directed anti-peptide antibodies which only bind to free peptides and not to parent precursor molecules." Hermon-Taylor, column 1, lines 19-24. In other words, the targets of the assays in Hermon-Taylor are trypsin activated peptides, *i.e.*, peptides specifically cleaved during the formation of

activated enzymes from zymogens. For example, the target for trypsinogen cleavage is a specific peptide with the amino acid sequence of YDDDDK. Since the assays of Hermon-Taylor recognize completely different peptides than that of the present invention, Hermon-Taylor cannot be said to anticipate mAbs that specifically bind canine cationic trypsin or canine cationic trypsinogen. Accordingly, Applicants respectfully request the withdrawal of this rejection.

**B. Guy-Crotte**

Claims 1-3 and 5-9 stand rejected under 35 U.S.C. § 102 (b), as allegedly anticipated by Guy-Crotte et al., EUR. J. BIOCHEM., 204:133 (1992) ("Guy-Crotte"). See June 25, 2003 Office Action, page 4. For the following reasons, Applicants respectfully traverse this rejection as applied to the amended claims.

Guy-Crotte fails to anticipate the claimed invention because the cited prior art reference fails to teach each and every element of the claimed invention. In particular, the mAb of Guy-Crotte does not selectively bind canine cationic trypsin nor canine cationic trypsinogen.

The G6 mAb of Guy-Crotte exhibits a different (*i.e.*, inferior) binding specificity when compared to those of the present invention. Specifically, the G6 mAb cross-reacts with both human trypsinogen 1 (*i.e.*, cationic trypsinogen) and human trypsinogen 2 (*i.e.*, anionic trypsinogen). See Guy-Crotte, page 136, 1st column, 2nd paragraph, last sentence to 2nd column, 1st paragraph, 1st sentence. By contrast, the mAbs of the present invention specifically recognize canine cationic trypsin, not canine anionic trypsin, nor human trypsins. See Specification, pages 47-48, Tables 1-2; page 57, Example 5, pages 65-66, Tables 7-9. In further support of this position, Applicants direct the Examiner's attention to the clinical test results attached as Appendix 1. As shown in Item 7 and Figure 5 of Appendix 1, the mAbs of the present invention recognize canine cationic trypsin, not bovine, porcine, nor canine anionic trypsins. These experimental results clearly demonstrate the superior specificity of the mAbs of the claimed invention.

Furthermore, Applicants note that the mAbs of the instant invention recognize an amino acid sequence of cationic trypsin even when Western Blotting is performed under reducing conditions. By contrast, the mAb in Guy-Crotte fails to recognize trypsin under reducing

conditions. See Guy-Crotte, page 135, 2nd column, 4th paragraph, last sentence to page 136, 1st column, 1st paragraph, 1st sentence. This further highlights the differences between the present invention and the teaching of Guy-Crotte.

Given the above-noted differences in the binding specificity between the mAb in the cited art and that of the claimed invention, Guy-Crotte cannot be said to anticipate the claimed invention. Thus, Applicants respectfully request the withdrawal of this rejection.

## VI. REJECTIONS UNDER 35 U.S.C. § 103

### A. Pinsky, Campbell, Harlow and Maurer

Claims 1-5, 8, and 9 stand rejected under 35 U.S.C. § 103(a), as allegedly unpatentable over Pinksy et al., MOL. CELL. BIOL., Vol. 5, No. 10, pp. 2669-2676 (1985) ("Pinsky"), in view of Campbell, MONOCLONAL ANTIBODY TECHNOLOGY. THE PRODUCTION AND CHARACTERIZATION OF RODENT AND HUMAN HYBRIDOMAS, Chapter 1: General properties and applications of monoclonal antibodies, pp. 1-4, 29 (Elsevier Science Publishers B.V., New York, 1984) ("Campbell (1984)"), Harlow et al., ANTIBODIES A LABORATORY MANUAL, Chapter 5, pp. 72-77 (Cold Spring Harbor Laboratory, Cold Spring Harbor, 1988) ("Harlow"), and Maurer et al., METHODS IN ENZYMOLOGY, Vol. 70, Chapter 2: Proteins and Polypeptides as Antigens, pp. 49-70 (Academic Press, Inc., 1980) ("Maurer"). See June 25, 2003 Office Action, pages 5-7.

Applicants respectfully traverse this rejection as applied to the amended claims for the following reasons.

To establish obviousness, three criteria must be met. First, the prior art references must teach or suggest each and every element of the claimed invention. See In re Royka, 490 F.2d 981, 180 U.S.P.Q. 580 (C.C.P.A. 1974); In re Zurko, 111 F.3d 887, 888-89, 42 U.S.P.Q.2d 1476, 1478 (Fed. Cir. 1997); In re Wilson, 424 F.2d 1382, 1385, 165 U.S.P.Q. 494, 496 (C.C.P.A. 1970); M.P.E.P. § 2143.03. Second, there must be some suggestion or motivation in the references to either modify or combine the reference teachings to arrive at the claimed invention. See In re Vaeck, 947 F.2d 488, 20 U.S.P.Q.2d 1438 (Fed. Cir. 1991); M.P.E.P. § 2143. Third, the prior art must provide a reasonable expectation of success. See Vaeck, 947

F.2d at 488, 20 U.S.P.Q.2d at 1438; In re Merck & Co., Inc., 800 F.2d 1091, 231 U.S.P.Q. 375 (Fed. Cir. 1986); M.P.E.P. § 2143.02.

In this case, the cited prior art references fail to teach and/or suggest each and every element of the claimed invention, namely, a mAb that selectively binds canine cationic trypsin and/or canine cationic trypsinogen, and immunoassay methods and kits thereto. Pinsky is the only cited reference to discuss canine trypsinogen. Although Pinsky discloses the sequences of the two major forms of canine trypsinogen, this reference does not disclose nor suggest Abs, let alone mAbs, that selectively bind canine cationic trypsin and/or canine cationic trypsinogen. Pinsky also fails to disclose immunoassay methods and kits for such.

Similarly, the secondary references of Campbell (1984), Harlow and Maurer also fail to disclose mAbs that selectively bind canine cationic trypsin and/or canine cationic trypsinogen and immunoassay thereto. These secondary references only discuss, in general terms, techniques for making Abs. Thus, the cited prior art fails to teach the mAbs and immunoassay of the present invention.

Furthermore, there is no suggestion and/or motivation in any of the references to make mAbs that selectively bind canine cationic trypsin or canine cationic trypsinogen. None of the references disclose the need and/or purpose for doing so. Instead, the Examiner presumes that there is motivation to do so based on the unfounded assertion that "canine trypsinogen proteins are of unquestioned research interest" and "it is conventional in the art to elicit antibodies to sequenced proteins for a variety of uses as taught in Campbell or Harlow et al. . . ." See Office Action, page 6, lines 12-14. However, the generalized teachings regarding Ab production in Campbell (1984) and Harlow never discuss nor suggest the importance of making of mAbs that selectively bind canine cationic trypsin or canine cationic trypsinogen, but do not bind canine anionic trypsin nor canine anionic trypsinogen. The mere fact that references can be combined and/or modified does not render the resultant combination obvious unless the prior art suggests the desirability of the combination. See In re Mills, 916 F.2d 680, 16 U.S.P.Q.2d 1430 (Fed. Cir. 1990); M.P.E.P. § 2143.01. Without further disclosure suggesting the purpose for doing so, the mere existence of a general method and/or technique for making of antibodies is insufficient to

provide a reason for making the mAbs of the present invention. Thus, the cited prior art references lack a suggestion to combine/modify the reference teachings to arrive at the claimed invention.

Thus, in view of the above, the claimed invention is not obvious over the cited references because the cited art references lack a suggestion to combine/modify the reference teachings to arrive at the claimed invention. Therefore, Applicants respectfully request the withdrawal of this rejection.

**B. Pinsky, Campbell, Harlow and Maurer**

Claims 6 and 7 stand rejected under 35 U.S.C. § 103(a), as allegedly unpatentable over Pinsky, Campbell (1984), Harlow, and Maurer, and further in view of Campbell, MONOCLONAL ANTIBODY AND IMMUNOSENSOR TECHNOLOGY. THE PRODUCTION AND APPLICATION OF RODENT AND HUMAN MONOCLONAL ANTIBODIES, Chapter 1: General properties and applications of monoclonal antibodies, pp. 3-6, and 45 (Elsevier Science Publishers B.V., New York, 1991) ("Campbell (1991)") and either Simpson et al., Am. J. Vet. Res. Vol. 50, No. 5, pp. 629, (1989) ("Simpson") or Borgström et al., HOPPE-SEYLER'S Z. PHYSIOL. CHEM., Vol. 361, pp. 625 (1980) ("Borgström"). See June 25, 2003 Office Action, pages 7-8.

Applicants respectfully traverse this rejection for the reasons for the same reasons discussed immediately above, and for the reasons set forth below.

Pinsky, Campbell (1984), Harlow, and Maurer are discussed above. To briefly reiterate, and as admitted by the Examiner, these references differ from the claimed invention in that they do not teach or suggest an immunoassay for determination of canine trypsinogen peptides. The Examiner relies on Borgström and Simpson as teaching immunoassays of canine trypsinogens for determination of pancreatitis. The Examiner further relies on Campbell (1991) as teaching general techniques for the production and use of monoclonal antibodies in immunoassays. However, none of these references teach and/or suggest mAbs that selectively bind canine cationic trypsin or trypsinongen.

Borgström also fails to teach and/or suggest mAbs that selectively bind canine cationic trypsin or trypsinongen, but do not bind canine anionic trypsin nor canine anionic trypsinogen.

Instead, Borgström performed radioimmunoassays ("RIA") to assay for canine cationic trypsin and canine anionic trypsin. Borgström also discusses the use of polyclonal Abs, not mAbs. Although Borgström mentions the use of "monospecific antisera", Borgström fails to discuss the methodology for preparing such Abs, let alone mAbs that selectively bind canine cationic trypsin or trypsinongen, but do not bind canine anionic trypsin nor canine anionic trypsinogen. Borgström fails to discuss the specificity of the "monospecific antisera." Thus, Borgström cannot suggest the method and kit of the claimed invention. Furthermore, there is no assessment in Borgström regarding clinical diagnosis, whereas through clinical trials using the present invention, it has been verified that the instant mAbs are highly useful for clinical applications, such as the diagnosis of dogs with exorcrine pancreatic insufficiency ("EPI") or pancreatitis.

Similarly, Simpson also fails to teach and/or suggest mAbs that selectively bind canine cationic trypsin or trypsinongen, but do not bind canine anionic trypsin nor canine anionic trypsinogen. Simpson also performed a RIA to assay for canine trypsin-like immunoreactivity ("TLI"). Nonetheless, Simpson fails to disclose mAbs, let alone mAbs that selectively bind canine cationic trypsin or canine cationic trypsinogen. Thus, Simpson cannot suggest the method and kit of the claimed invention. Also, there is no assessment in Simpson regarding clinical diagnosis. Simpson only determines the concentration of dog cationic trypsin using RIA after experimental ligation of the pancreatic ducts of dogs. Simpson does not provide clinical data for diagnostic applications. By contrast, as shown in Figure 3 of Appendix 1, the mAbs of the instant invention are highly useful for the clinical diagnoses of dogs for exocrine pancreatic insufficiency ("EPI") or pancreatitis. Thus, the instant mAbs are highly useful for clinical applications.

The Examiner relies on Campbell (1991) as teaching general techniques for the production of mAbs and their use in immunoassays. The Examiner alleges that it would have been obvious to make and use mAbs for the immunoassays disclosed in the prior art "in order to make use of a potentially unlimited source of homogenous reagent to standardize the assay." See June 25, 2003 Office Action, page 8. However, this amounts to nothing more than an improper obvious to try rationale. In moving from the prior art to the claimed invention, one cannot base a determination

of obviousness on what one of ordinary skill in the art might try or find obvious to try. In re O'Farrel, 7 U.S.P.Q.2d 1673, 1681, (Fed. Cir. 1988).

Thus, in view of the above, the claimed invention is not obvious over the cited references because the cited art references lack a suggestion to combine/modify the reference teachings to arrive at the claimed invention and do not contain a reasonable expectation of success at arriving at the claimed invention. Therefore, Applicants respectfully request the withdrawal of this rejection.

## CONCLUSION

For at least the foregoing reasons, Applicants respectfully submit that the present patent application is in condition for allowance. An early indication of the allowability of the present patent application is therefore respectfully solicited.

If Examiner Grun believes that a telephone conference with the undersigned would expedite passage of the present patent application to issue, he is invited to telephone on the undersigned at the number below.

Respectfully submitted,

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